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Further Studies on the Oxy-functionalization of Cholesteryl Acetate with *tert*-Butyl Hydroperoxide and Tris(acetylacetonato)iron(III)[1)]

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The time courses of the spectral change, decomposition, and consumption of Fe(acac)$_3$, *tert*-butyl(^{t}Bu) hydroperoxide, and cholesteryl acetate, respectively, in the title reaction were followed and the reaction was inferred to be initiated by the active species originating from the interaction of the ferric chelate and the hydroperoxide. Radical processes seem to participate in this reaction, since it was completely inhibited by a radical scavenger (BHT), which was also effective in blocking the further transformation of the intermediary C(7)-^{t}Bu-peroxide. The ^{t}BuBr–KO$_2$ system generating ^{t}BuOO· radicals oxidized cholesteryl methylether almost exclusively to an epoxide. The ^{t}BuOOH–KO$_2$ system generating ^{t}BuO· radicals, on the other hand, abstracted the allylic C(7)-hydrogen to give the ^{t}Bu-peroxide, the alcohol, and the ketone, but no epoxide. The intermediary ^{t}Bu-peroxide was assumed to be produced also by the nucleophilic attack of ^{t}BuOOH on the allylic cation, to which the initially formed C(7)-radical species was further oxidized.

A proposed mechanism is presented for the title reaction.

Keywords——alkylperoxy and alkoxy radicals; allylic oxidation; dialkylperoxide; epoxidation; hydroxylation; product distribution; solvent effect; stilbene; time course of reaction

In the studies of this series, we have shown that the reaction of cholesteryl acetate (**1**) with the system involving *tert*-butyl hydroperoxide(^{t}BuOOH) and tris(acetylacetonato)-iron(III), Fe(acac)$_3$, in benzene gave 7-*tert*-butylperoxycholest-5-en-3β-ol acetate (**2**), 3β-acetoxycholest-5-en-7-ol (**3**), 3β-acetoxycholest-5-en-7-one (**4**), and 5,6-epoxycholestan-3β-ol acetate (**5**), with predominant allylic oxidation.[2)] The major final product, **4**, was assumed to be formed through the intermediate **2**. Epoxidation and allylic oxidation of **1** were also studied with hydroperoxides of different type (ROOH: R=H, ethyl, iso-propyl, *tert*-butyl, or cumenyl) and Fe (acac)$_3$.[3)] The stereoselective β-epoxidation of **1** was independent of the structure of ROOH, but the ratio of allylic oxidation to epoxidation was dependent upon it. When the non-polar solvent, benzene, was replaced with a polar one, acetonitrile, the ratio of β-epimer to the total epoxide (**5**) and that of allylic oxidation to epoxidation remained almost unchanged for a given alkyl hydroperoxide. In the reactions of **1** with ^{t}BuOOH and an acetylacetonate of a transition metal such as TiO(II), VO(II), Cr(III), Mn(II, III), Co(II, III), Ni(II), Cu(II), MoO$_2$(II), or Ce(III), the product distribution was rather similar to that in the reaction catalyzed by Fe(acac)$_3$, except in the case of MoO$_2$(acac)$_2$ where the epoxidation was strongly predominant.[1b)] The effects of metal valency, ligand group, and solvent, as well as of radical scavenger were then examined in the reactions of **1** with ^{t}BuOOH and molybdenum complexes. The results of these studies on the mechanism prompted us to reinvestigate the reactions catalyzed by Fe(acac)$_3$. In this study, we observed the title reaction in various types of solvent and with systems generating *tert*-butoxy(^{t}BuO·) and -butylperoxy (^{t}BuOO·) radicals. Radical and in part, ionic mechanisms are proposed for the title reaction.

Results and Discussion

Time Course of the Reaction Profile

Spectral change of the iron chelate, decomposition of the hydroperoxide, and oxidation of the substrate (**1**) did not occur in the mixture of **1**, ^{t}BuOOH, Fe(acac)$_3$, and benzene at room temperature. The iron chelate was also stable in boiling benzene. However, the absorption spectrum of Fe(acac)$_3$ changed under the cited reaction conditions (reflux under an argon atmosphere)[2,3] and the maximum at 436 nm was lost after 60 min (Fig. 1). The consumption of **1** was initiated simultaneously with rapid decomposition of the iron chelate, as shown in Fig. 2. The same figure indicates that the decomposition of ^{t}BuOOH was accelerated at the period when most of the Fe(acac)$_3$ was decomposed. The reaction of **1** also occurred when it was added to the reagent system, in which the decomposition of Fe(acac)$_3$ had arrived at an apparent final state. Destructive autoxidation of Fe(acac)$_3$ was assumed to include the equilibrium: Fe(acac)$_3 \rightleftharpoons$ (acac)· + Fe(acac)$_2$, and coupling of the acetylacetone radicals with dioxygen species resulted in the formation of biacetyl, acetic acid, carbon dioxide, and water.[4] The decomposition of cumenyl hydroperoxide in the presence of Co(acac)$_2$ proceeded *via* the formation of an intermediate complex of hydroperoxide and metal compound, which decayed exclusively into free radicals.[5] It may, therefore, be reasonable to assume that the oxidation of **1** was initiated by active species formed through the interaction of Fe(acac)$_3$ with ^{t}BuOOH.

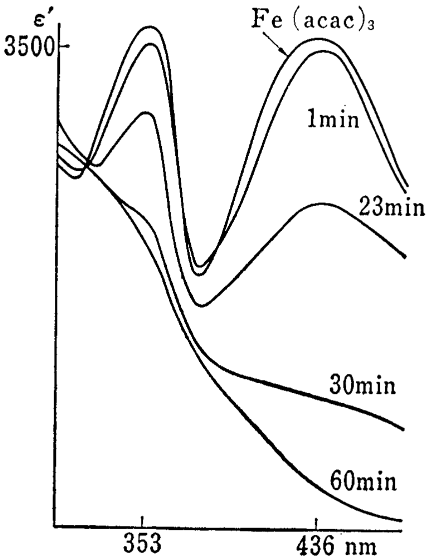


Fig. 1. Changes in the Spectrum of the Reaction Mixture with Time

Conditions: benzene (20 ml), cholesteryl acetate (1.2 mmol), Fe(acac)$_3$ (0.13 mmol), ^{t}BuOOH (9.2 mmol), refluxed under an Ar atmosphere.

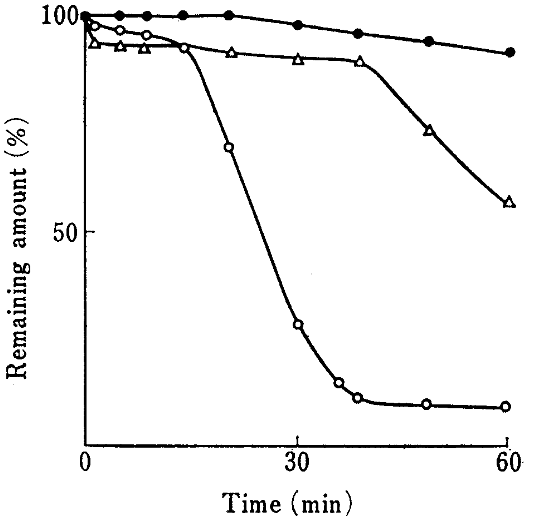


Fig. 2. Relation between Oxidation of Cholesteryl Acetate and Decomposition of Fe(acac)$_3$ and ^{t}BuOOH

—●—: cholesteryl acetate, —○—: Fe(acac)$_3$, —△—: ^{t}BuOOH.

The Reaction in Various Solvents

In the reaction of **1** in the ^{t}BuOOH–Mo(CO)$_6$ system, epoxidation and allylic oxidation proceeded exclusively in benzene and ^{t}BuOH, respectively but acetonitrile differently affected the reaction; the epimer ratios of the epoxide (**5**) were also different in these solvents.[1b] In contrast, the product distributions were similar when the molybdenum catalyst was replaced by Fe(acac)$_3$ in these solvent systems, and the results are summarized in Table I. It is noteworthy that the product distributions in the title reaction were analogous to those obtained with the ^{t}BuOOH–Mo(CO)$_6$ system in ^{t}BuOH, where radical reactions were proposed to proceed.[1b]

Acetonitrile was also distinctive as a solvent in the present iron-catalyzed reaction, where consumption of the substrate (**1**) was low and the residual level of the intermediary 7-*tert*-butylperoxycholest-5-en-3β-ol acetate (**2**) was high. The species ^{t}BuOO$^-$, ^{t}BuOO· and ^{t}BuO· are known to attack nitrile compounds, and the hydroperoxide is readily consumed by the

TABLE I. Effect of Solvent on the Product Distribution[a]

Solvent	Conversion (%)	Yield (%) Epoxide[b] 5	C(7)-one 4	C(7)-OH 3	C(7)-Peroxide 2	Allylic oxidation (%)
C_6H_6	100	13(0.72)	74	3	11	87
CH_3CN	42	4(0.72)	8	0	30	90
${}^tBuOH$	96	7(0.75)	61	3	25	93
$Mo(CO)_6$ in ${}^tBuOH$[1b]	90	11(0.78)	66	2	11	88

a) Data are the means of three runs.
b) Numbers in parentheses are ratios of β-epoxide to the total epimers formed.

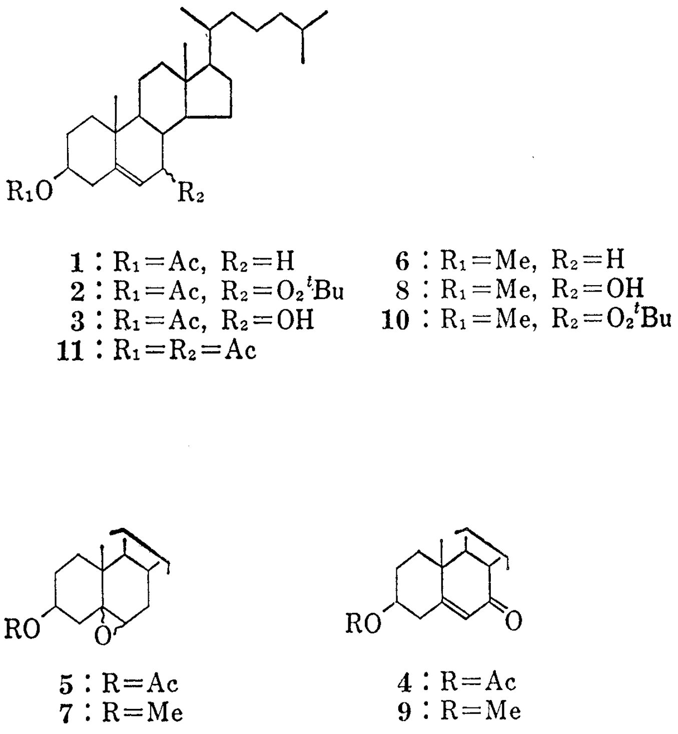
subsequent chain reactions.[6] The low conversion of **1** may, therefore, be due to the reduced concentration of ${}^tBuOOH$.

Epoxidation of Stilbenes

In the epoxidation of stilbene by a radical process, the intermediate can rotate around the attacked C–C bond and thus attain conformational equilibrium.[7] Formation of such a radical intermediate should, therefore, mean that *cis*- and *trans*-stilbenes would both give epoxide mixture with similar isomeric ratios. Epoxidations of these stilbenes by the ${}^tBuOOH$–$Mo(CO)_6$ system in ${}^tBuOH$ did give the same isomeric ratio of *trans*: *cis*=9: 1.[1b] The ${}^tBuOOH$–$Fe(acac)_3$ system in benzene showed a similar ratio of 96: 4, as expected.

Effect of Radical Scavenger

Radicals such as ${}^tBuO\cdot$ and ${}^tBuOO\cdot$ are known to be produced from ${}^tBuOOH$ through its metal-catalyzed[8] and radical-induced[9] decomposition. The radical scavenger BHT inhibited the molbdenum-catalyzed reaction in ${}^tBuOH$ but it was entirely inert in benzene



1: R_1=Ac, R_2=H
2: R_1=Ac, R_2=$O_2{}^tBu$
3: R_1=Ac, R_2=OH
11: R_1=R_2=Ac

6: R_1=Me, R_2=H
8: R_1=Me, R_2=OH
10: R_1=Me, R_2=$O_2{}^tBu$

5: R=Ac
7: R=Me

4: R=Ac
9: R=Me

Chart 1

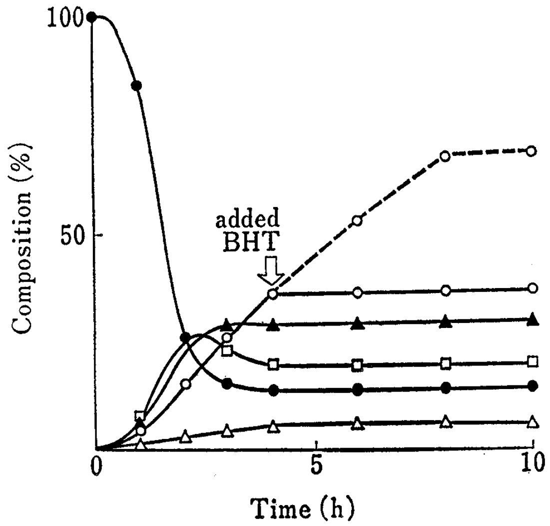


Fig. 3. Effect of BHT on the Decomposition of C(7)–Alkylperoxide

—●—: cholesteryl acetate, —○—: C(7)-one, —△—: C(5,6)-epoxide, —▲—: C(7)α-peroxide, —□—: C(7)β-peroxide, ···○···: C(7)-one without BHT.

medium.[1b] Since BHT inhibited the oxidation of **1** by the ^{t}BuOOH–Fe(acac)$_3$ system in benzene, radical processes seem to dominate in the title reaction. The allylic oxidation in the title reaction was assumed to proceed *via* an intermediary peroxide (**2**), which was then transformed into the alcohol (**3**) and the ketone (**4**).[2] As shown in Fig. 3, BHT was also effective for inhibiting the transformation of **2**.

Reactions by the Alkylperoxy and Alkoxy Radicals

Homolytic decomposition of alkyl hydroperoxide by a metallic catalyst is known to proceed as shown below:[10]

$$M^{n+} + \mathrm{ROOH} \longrightarrow M^{(n+1)+} + \mathrm{RO}^{\cdot} + \mathrm{OH}^-$$

$$M^{(n+1)+} + \mathrm{ROOH} \longrightarrow M^{n+} + \mathrm{ROO}^{\cdot} + \mathrm{H}^+$$

Participation of *tert*-butylperoxy as well as *tert*-butoxy radicals in the title reaction may, therefore, be reasonably assumed.

Table II. Oxidation of Cholesteryl Methylether with ^{t}BuOO and ^{t}BuO.[a]

	Yield (%)			
	Epoxide[b] **7**	C(7)–One **9**	C(7)–OH **8**	C(7)–Peroxide **10**
^{t}BuBr–KO$_2$	14(0.75)	0	Trace	0
^{t}BuOOH–KO$_2$	0	1	2	6

[a] Data are the means of three runs.
[b] Numbers in parentheses are ratios of β-epoxide to the total epimers formed.

A mixture of alkyl bromide and superoxide anion is regarded as a good generator of alkylperoxy radicals.[11] The reaction of cholesteryl methylether (**6**)[12] with ^{t}BuOO· gave the C(5,6)-epoxide (**7**) with a trace of the C(7)-alcohol (**8**). The epimeric distribution of the epoxide was determined to be 0.75 ($\beta/\alpha+\beta$), which is fairly consistent with the stereoselectivity shown in the epoxide (**5**) formation of **1** by the ^{t}BuOOH–Fe (acac)$_3$ system (Table II). It seems, therefore, that ^{t}BuOO· can act as an epoxidizing agent of olefins. Formation of **8** might be due to coexisting ^{t}BuO·.

The reaction of **6** with ^{t}BuO· generated from the mixture of *t*BuOOH and KO$_2$ in acetonitrile,[13] yielded **8**, the C(7)-ketone (**9**), and the C(7)-alkylperoxide (**10**) (Table II) but no epoxide (**7**) was detectable. It may be assumed from these results, as summarized in Table II, that ^{t}BuO· is exclusively responsible for the abstraction of allylic hydrogen. Formation of **10** may be due to the subsequent coupling of the allylic radical with ^{t}BuOO·, which was reported to coexist in the reaction mixture of ^{t}BuOOH and KO$_2$ in CH$_3$CN.[6a]

The intermediary peroxide **2** in the title reaction was found to be transformed into **4** without any trace of the epoxide **5**,[2] and BHT inhibited the reaction as described above. Decomposition of a primary or secondary alkylperoxide into the carbonyl compound proceeds *via* abstraction of the hydrogen on the α-carbon atom adjacent to the peroxy function.[14] The only product in the reaction of the peroxide **10** with ^{t}BuO· or ^{t}BuOO was the ketone **9**, as expected, and the yield was 11.6 or 5.7%, respectively.

The C(7)-ketone **4** was also obtained almost quantitatively from the C(7)-alcohol **3** when it was treated with the ^{t}BuOOH–Fe(acac)$_3$ system. It may be reasonable to assume that the allylic alcohol **3** can be further oxidized by the radical species produced in the title reaction.

Formation of the Dialkylperoxide *via* Oxidation of the Allylic Radical

Dialkylperoxide can be synthesized by the metal-catalyzed reaction of an olefin with a hydroperoxide. After abstraction of the allylic hydrogen, the reaction proceeds *via* the following pathway (s):[15] (1) coupling of the allylic radical with alkylperoxy radical and/or

(2) one-electron oxidation of the allylic radical into the allylic cation, which is subsequently attacked by the hydroperoxide as a nucleophile. In fact, the allylic acetate was isolated when the reaction was carried out in acetic acid.[16] The title reaction in benzene was thus carried out in the presence of acetic acid, and formation of the C(7)-acetate (**11**) was noted, as expected. It may, therefore, be reasonable to assume that the intermediary diakylperoxide (**2**) was produced, probably in part, *via* an allylic cation.

Mechanism

From these results, the mechanism of the title reaction may be rationalized on the basis of the scheme shown in Chart 2.

$$Fe^{2+} + ROOH \longrightarrow Fe^{3+} + RO\cdot + OH^-$$
$$Fe^{3+} + ROOH \longrightarrow Fe^{2+} + ROO\cdot + H^+$$

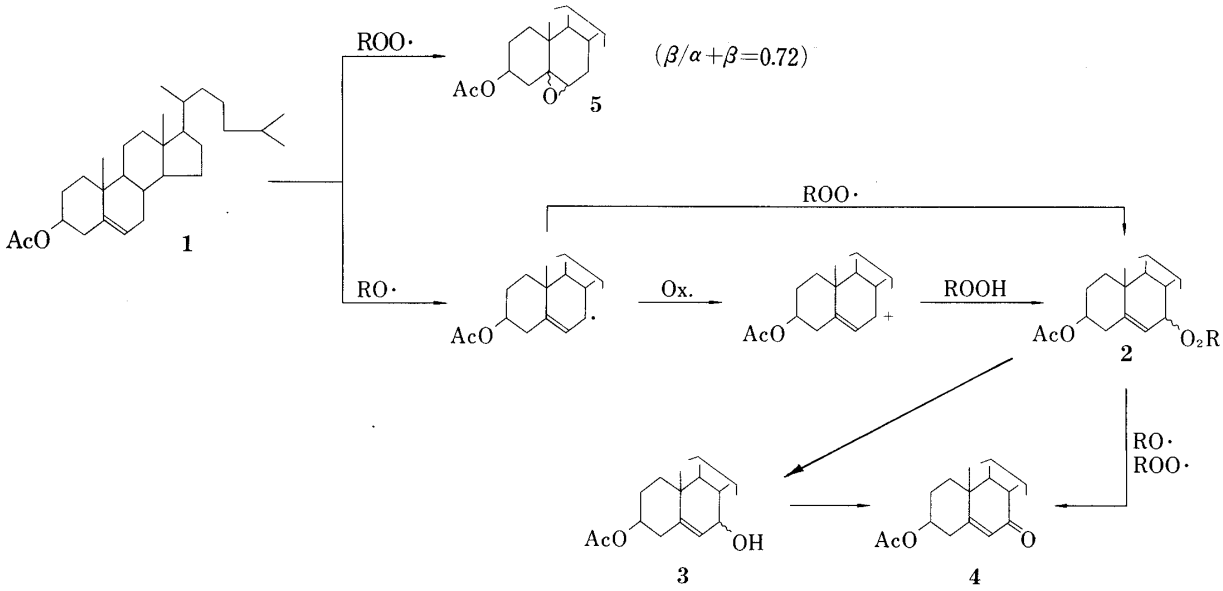


Chart 2. Mechanism of the Fe(acac)$_3$–Catalyzed Oxidation of Cholesteryl acetate with ROOH

Experimental

General Methods——Melting points were taken on a micro hot-stage apparatus and are uncorrected. Thin-layer chromatography (TLC) was carried out on silica gel (Wako-gel B5F) plates developed, unless otherwise noted, with PhH/AcOEt (19: 1) and stained with 10% H_2SO_4, with heating at about 130°C for 5 min. Ultraviolet (UV) spectra were taken on a Shimadzu UV220 spectrometer. Gas chromatograms were taken on a Shimadzu GC4A machine. Proton magnetic resonance (PMR) spectra were measured with a JEOL JNM-FX 100 FT spectrometer at 100 MHz with tetramethylsilane as an internal standard in $CDCl_3$. The general procedure for the title reaction was the same as that previously reported.[2,3] Determination of the product distribution and the epimeric ratio of the epoxide in the reaction mixture were carried out by the reported methods using an Iatron TFG-10 Thinchrograph (TLG-FID)[2] and PMR spectrometer,[3] respectively.

Materials and Authentic Specimens——Fe (acac)$_3$ (mp 183°C, lit.[17a] 182°C; Wako Pure Chem. Ind. Ltd.), BHT [2,6-di-*tert*-butyl-*p*-cresol] (Wako Pure Chem. Ind. Ltd.), *trans*- and *cis*-stilbenes (Aldrich Chem. Company, Inc.), dicyclohexyl-18-crown-6 (Nippon Soda Campany, Ltd.), KO_2 (96.5%; Alfa Division), and *tert*-BuBr (Wako Pure Chem. Ind. Ltd.) were obtained commercially and used without purification. *tert*-Butylhydroperoxide (Nakarai Chem. Co.) was purified by distillation under reduced pressure and its purity (98%) was determined by iodometry. Cholesteryl acetate (**1**, mp 117—118°C, lit.[17b] 116°C), 3β-methoxycholest-5-ene (**6**, mp 82.5—84°C, lit.[17c] 84.5—85.5°C), 3β-acetoxycholest-5-en-7-one (**4**, mp 154—156°C, lit.[17d] 157—158°C), 3β-methoxycholest-5-en-7-one (**9**, mp 121—123°C, lit.[17e] 120—122°C), 7α-*tert*-butylperoxycholest-5-en-3β-ol acetate (**2a**, mp 112—113°C, lit.[2] 112—113°C), and 7β-*tert*-butylperoxycholest-5-

en-3β-ol acetate (**2b**, mp 101.5—102.5°C, lit.[2] 101.5—102.5°C) were prepared by the cited methods. 3β-Acetoxycholest-5-en-7-ol (**3**, epimeric mixture) and 3β-methoxycholest-5-en-7-ol (**8**, epimr. mixt.) were prepared by reducing the corresponding C(7)-ketones with $NaBH_4$. Cholest-5-ene-3β,7-diol diacetate (**11**, epimr. mixt.) was prepared by acetylating **3** (epimer. mixt.) in Ac_2O–pyridine. 7-*tert*-Butylperoxy-3β-methoxycholest-5-ene (**10**, epimer. mixt.) was obtained from the reaction mixture of **6** and the ^{t}BuOOH-Fe(acac)$_3$ system. 5,6-Epoxycholestan-3β-ol acetate (**5**, epimer. mixt.) and 5,6-epoxy-3β-methoxycholestane (**7**, epimer. mixt.) were prepared by the epoxidation of **1** and **6** with *m*-chloroperbenzoic acid, respectively.

Time Course of the Reaction Profile——Consumption of Fe(acac)$_3$ (Figs. 1 and 2): A benzene solution (50 ml) of **1** (500 mg, 1.17 mmol), ^{t}BuOOH (1 ml, 9.8 mmol), and Fe(acac)$_3$ (41.9 mg, 0.12 mmol) was treated according to the general procedure (reflux under an Ar atmosphere).[2,3] At each specified time, 2 ml of the reaction mixture was sampled and made up to 10 ml with benzene. The amount of Fe(acac)$_3$ remaining was determined by measuring the absorption at 353 (ε, 3820) and 436 (3650) nm.

Consumption of ^{t}BuOOH (Fig. 2): A benzene solution (5 ml) of **1** (50 mg, 0.12 mmol), Fe(acac)$_3$ (4.20 mg, 1.2×10^{-2} mmol), and ^{t}BuOOH (0.1 ml, 0.98 mmol) was treated as described above. At each specified time, 0.1 ml of the reaction mixture was sampled, 1 μl of chlorobenzene was added as an internal standard, and finally 1 μl of the sample solution was subjected to gas–liquid chromatography (GLC), to determine the amount of ^{t}BuOOH remaining. GLC conditions: stainless steel column (1.5% SE52, 3 mm$\phi\times$2 m); temp. (70°C for injection, 30°C for column, 70°C for detector); carrier gas (N_2, 60 ml/min); t_R(^{t}BuOOH, 3 min; chlorobenzene, 5 min); relative sensitivity (^{t}BuOOH, 0.42; chlorobenzene, 1.00).

Consumption of Cholesteryl Acetate (Fig. 2): A benzene solution (5 ml) of Fe(acac)$_3$ (4.20 mg, 1.2×10^{-2} mmol), ^{t}BuOOH (0.1 ml, 0.98 mmol), and **1** (50 mg, 0.12 mmol) was treated as described above. The remaining amount of **1** in the reaction mixture was determined at each specified time by the TLC–FID method.[18]

Effect of Solvent on the Reaction (Table I)——A mixture of **1** (50 mg, 0.12 mmol), Fe(acac)$_3$ (4.20 mg, 1.2×10^{-2} mmol), and ^{t}BuOOH (0.1 ml, 0.98 mmol) was dissolved in the solvent (5 ml) and treated as described above. The epoxide (**5**) was separated by preparative TLC. Its yield was 6.5, 2.2, or 3.1 mg in benzene, acetonitrile, or ^{t}BuOH, respectively. The consumption of **1** and the product distribution were determined by the TLC–FID method.

Epoxidation of Stilbene——The reaction of *trans*- or *cis*-stilbene (40 mg, 0.24 mmol) with Fe(acac)$_3$ (8.2 mg, 2.4×10^{-2} mmol) and ^{t}BuOOH (0.2 ml, 1.96 mmol) was carried out in benzene (10 ml). The yield was determined by the TLC–FID method (solvent system, *n*-hexane/PhH=3/1, triple development; stilbene, *Rf* 0.75; stilbene oxide, *Rf* 0.40). The epimeric ratio of the epoxide was determined by measuring the peak areas of the protons attached to the epoxide carbons.

Effect of Radical Scavenger on the Reaction——1. According to the general procedure, a mixture of **1** (50 mg, 0.12 mmol), Fe(acac)$_3$ (4.20 mg, 1.2×10^{-2} mmol), and ^{t}BuOOH (0.1 ml, 0.98 mmol) was treated in benzene (5 ml) containing various amounts of BHT, such as 15 mg (6.5×10^{-2} mmol, 1.3×10^{-2} M), 26 mg (1.2×10^{-1} mmol, 2.4×10^{-2} M), and 660 mg (3 mmol, 6.0×10^{-1} M). The product distributions were determined by the TLC–FID method, with the following results:

BHT (M)	Consumption (%)	Yield (%)			
		2	**3**	**4**	**5**
0	100	11	3	74	13
1.3×10^{-2}	80	41	3	30	6
2.4×10^{-2}	37	26	1	6	4
6.0×10^{-1}	0	Trace	0	Trace	0

2 (Fig. 3). A mixture of **1**, Fe(acac)$_3$, ^{t}BuOOH, and benzene in the same amounts as cited above was similarly treated for 4 h. BHT (135 mg, 0.59 mmol) was then added to the reaction mixture, which was refluxed for another 20 h under an Ar atmosphere. The product distribution was determined at each specified time by the TLC–FID method. *Rf* values with the solvent system PhH: AcOEt=19: 1: **1** (0.75), **2** (0.75), **3** (0.35), **4** (0.40), **5** (0.52); with the solvent system *n*-hexane: PhH=4: 6 (triple development): **1** (0.50), **2** (7α-epimer, 0.20; 7β-epimer, 0.30), **3** (0.00), **4** (0.00), **5** (0.00).

Reactions by the Alkylperoxy Radicals (^{t}BuOO·)——I (Table II). A benzene solution (1 ml) of KO_2 (800 mg, 47 mmol) and dicyclohexyl 18-crown-6 (186 mg, 0.5 mmol) was mixed with a benzene solution (4 ml) of cholesteryl methylether (**6**, 500 mg, 1.25 mmol) and finally with ^{t}BuBr (0.5 ml, 4.5 mmol). After the mixture had been vigorously stirred for 10 h at room temperature with a $CaCl_2$ tube attached for drying, water (5 ml) was added to decompose the remaining KO_2. The benzene layer was combined with the ether solution obtained by extracting the aqueous layer 3 times with fresh ether, and the mixture was washed with 2 N HCl, 5% aq. $NaHCO_3$, and saturated aq. NaCl, then dried over anhydrous Na_2SO_4. Evaporation of the solvent from the organic solution gave a residue, which was subjected to chromatography on silica gel (10 g, eluted with 200 ml of $CHCl_3$) to remove the crown ether. The $CHCl_3$ eluate was evaporated to dryness and the residue (493 mg) was subjected to preparative TLC to give 70 mg of the epoxide fraction. A small amount of the residue was used to determine the product distribution by the TLC–FID method. No reaction occurred in the control solution lacking ^{t}BuBr.

2. A benzene solution (4.5 ml) of the 7-butylperoxide (**10**, 21.3 mg, 4.36×10^{-2} mmol; an epimeric mixture of $7\alpha:7\beta=1:1$), a benzene solution (1 ml) of KO_2 (50.7 mg, 0.71 mmol) and dicyclohexyl 18-crown-6 (40.5 mg, 0.11 mmol), and ^{t}BuBr (0.2 ml, 1.75 mmol) were treated as described above. After work-up as usual, the reaction mixture finally gave a residue (20.1 mg), which was used to determine the product distribution by the TLC–FID method. The conversion was 5.7% and the only product was the ketone **9**. No reaction occurred in the control solution lacking ^{t}BuBr.

Reactions by the Alkoxy Radicals (^{t}BuO•)——1 (Table II). A CH_3CN solution (1 ml) of KO_2 (800 mg, 47 mmol) and dicyclohexyl 18-crown-6 (185 mg, 0.1 mmol), a CH_3CN solution (9 ml) of **6** (500 mg, 1.25 mmol), and ^{t}BuOOH (0.5 ml, 4.9 mmol) were treated as above and the reaction mixture, after work-up as usual, finally gave a residue (501 mg), whose product distribution was determined by the TLC–FID method. No reaction occurred in the control lacking ^{t}BuOOH.

2. A CH_3CN solution (1 ml) of KO_2 (50.2 mg, 0.71 mmol) and dicyclohexyl 18-crown-6 (4.0 mg, 1.1×10^{-2} mmol), a CH_3CN solution (4 ml) of **10** (40.0 mg, 8.20×10^{-2} mmol), and ^{t}BuOOH (0.03 ml, 0.37 mmol) were treated as described above and the reaction mixture, after work-up as usual, finally gave a residue (49 mg), whose product distribution was determined by the TLC–FID method. The conversion was 11.6% and the only product was the ketone **9**. No reaction occurred in the control lacking ^{t}BuOOH.

The Title Reaction in the Presence of Acetic Acid——A benzene solution (3 ml) of **1** (50 mg, 0.12 mmol), $Fe(acac)_3$ (4.10 mg, 1.2×10^{-2} mmol), ^{t}BuOOH (0.1 ml, 0.98 mmol), and acetic acid (2 ml, 34 mmol) was treated according to the general procedure. The reaction mixture was then directly subjected to TLC and formation of the diacetate (**11**) was confirmed by comparing its *Rf* value (0.70 in the solvent system PhH: AcOEt=19: 1; 0.10 in the solvent system *n*-hexane: PhH=4: 6, triple development) with that of an authentic specimen (7α-epimer: mp 120—121°C, lit.[17f] 122°C; 7β-epimer: mp 107—109°C, lit.[17f] 108—110°C).

Oxidation of the C(7)-Hydroxide (3) by the ^{t}BuOOH-$Fe(acac)_3$ System——A benzene solution (5 ml) of **3** (51.7 mg, 0.12 mmol), and epimeric mixture of $7\alpha:7\beta=1:6$), $Fe(acac)_3$ (4.2 mg, 1.2×10^{-2} mmol), and ^{t}BuOOH (0.10 ml, 0.98 mmol) was treated as above. The reaction mixture was then directly subjected to TLC and formation of the C(7)-ketone (**4**) was confirmed and estimated by comparing its *Rf* value (0.40 in the solvent system PhH: EtOAc=19: 1; 0.00 in the solvent system *n*-hexane: PhH=4: 6, triple development) with that of an authentic specimen and by the TLC–FID method, respectively.

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References and Notes

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18) A benzene solution of $Fe(acac)_3$ (1.2×10^{-2} mmol) and ${}^{t}BuOOH$ (0.98 mmol) was refluxed under an Ar atmosphere for 40 min, by which time the decomposition of the iron chelate had arrived at an apparent final state, as shown in Fig. 2. Then, **1** (0.12 mmol) was added to the reaction mixture and the remaining amounts of **1** in the boiling solution were similarly determined after 1, 3, 10, 30, and 60 min. The lag-time that was observed in the conversion of **1** (Fig. 2) was lost in this case and the oxy-functionalization of **1** proceeded rapidly.